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THE TREATMENT OF WASSERMANN-FAST SYPHILIS

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DISCUSSION. JANUARY 31st, 1930

THE PRESIDENT said he was sure all present would feel they had just listened to a very interesting paper on a very important subject, and that they would wish him to thank Colonel Burke for having come to submit it to the Society for discussion. The speaker congratulated the reader both on the matter in the paper and on his method of delivering it.

He was certain that it would provoke a good deal of debate, and, therefore, though it would be tempting to do so, he hoped speakers would not dwell much on the question as to whether mercury should be given at the same time as arsenobenzol compounds or in a separate course, but would mainly adhere to the subject-matter of Colonel Burke's contribution.

Colonel HARRISON congratulated Colonel Burke on his excellent paper, with most of which he agreed heartily. Although the President had expressed a wish to avoid any side issue such as the question of concurrent versus alternating arsenobenzene and bismuth or mercury, he felt he must take up Colonel Burke's challenge, particularly as Colonel Burke had said that the concurrent method led to Wassermann-fastness. He (Col. H.) thought a much more important issue was the question whether the alternating method, giving first a course of arsenobenzene, then one of mercury or bismuth, and so on, in early cases, led to more neuro-syphilis. He felt strongly that it did. He was glad to find that Colonel Burke did not favour the purely arsenobenzene treatment. As was well known, in a number of quarters it had been stated that the modern treatment of syphilis led to more and earlier neuro-syphilis. In this country they had tried to obtain a decision on the question by an inquiry to discover if many of the survivors of the 100,000

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soldiers treated for syphilis during the War had been seen later at neurological or V.D. clinics, in Pensions Hospitals, or in certain Mental Hospitals, suffering from neuro-syphilis. They had not been able to discover evidence in this material supporting the idea that neuro-syphilis had increased under modern methods of treating syphilis, as they had found only six cases. However, there was no smoke without some fire behind it, and he had been interested in trying to discover in what ways the treatment given to our syphilitic soldiers during the War had differed from that given to patients of syphilologists who maintained that modern treatment did increase neuro-syphilis, and he thought it lay in the fact that our soldiers had been treated on the concurrent plan. In support, he would quote from a few articles he had reviewed. Alurralde and Sepich (*Bull. Office Int. d'Hgy. Pub.*, 1928, v. 20, p. 1951) were strongly of opinion that neuro-syphilis had increased in Brazil, and attributed it to the common practice of using arsenobenzene compounds exclusively. In a paper by Weatherby (*A. J. Syph.*, 1929, v. 13, p. 339), on the previous treatment of 280 patients who had developed neuro-syphilis, out of five whose treatment had commenced in the primary stage, all but one had received arsenobenzene alone, and the single exception had received arsenobenzene with only three doses of mercury. Out of nine treated in the secondary stage, four had received only arsenobenzene, and one mercury only. Bernard (*Brux. Med.*, 1928, v. 8, p. 1602) had tested the fluid of 200 patients and related the findings to previous treatment. The fluid had been pathological in seventy-five out of eighty-nine treated with arsenobenzene only; in fourteen out of thirty-four treated on the principle of alternating courses of arsenobenzene and mercury; and in only three out of forty-two cases treated with arsenobenzene and mercury concurrently. In the analysis of cases treated at St. Thomas's Hospital which the Medical Research Council had published, he had contrasted the experience in respect of clinically manifest neuro-recurrence in the cases which had been treated there with that of Moore and Kemp, who treated rather more intensively, but on the alternating plan. He thought it reasonable to suppose that, when an early case was treated first with arsenobenzene, the spirochæte tended to settle in the nervous system, and got a start of eight weeks in doing so,

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before the mercury or bismuth, with its perhaps more penetrating and certainly more persistent action, was introduced. Colonel Burke had deprecated the bombardment of the tissues with two metals, but he used silver-salvarsan, which arose from Ehrlich's idea that one would be more likely to destroy the spirochæte with two poisons than with one. Colonel Burke, if he understood him rightly, had suggested that the germ had a better chance of becoming tolerant of the drugs if both were given at the same time. He (Col. H.) confessed he could not follow the reasoning of this. In any case there was no sound experimental evidence to show that the spirochæte did become tolerant. Colonel Burke had blamed the concurrent method for Wassermann-fastness, but in his (Col. H.'s) experience, the most intractable cases from this point of view had been patients who had received little or no treatment for a number of years. He thought that probably Wassermann-fastness depended mostly on inaccessibility of the parasites, and believed strongly in the free use of iodides in these cases. The tissues were certainly a very important factor in the cure of syphilis, but another was the remedy and its method of administration. He would be sorry if Colonel Burke had converted any one of the audience to the alternating plan, because he felt strongly that if this became popular, neuro-syphilis would increase in this country.

Dr. ANWYL DAVIES said he had thoroughly enjoyed Colonel Burke's paper, and extended his congratulations to him. He asked whether the opener had had any experience of the effect of sodium thiosulphate on the Wassermann reaction. A paper appeared in an American journal in 1928 reporting 28 cases with a persistently positive Wassermann, and in 10 it became negative after using sodium thiosulphate. The speaker's own results of employing it were not as good as those.

He was interested in Colonel Burke's statement that protein shock therapy raised the patient's immunity. He, Dr. Davies, felt doubtful about that. His view was that protein shock, at least as far as the gonococcus was concerned, lowered the immunity, and after those methods it took a longer time to bring about a cure.

Dr. RIDDOCH said that the subject under discussion is most important, but impossible at present to settle because of our imperfect pathological knowledge. The

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future may show that there is more than one cause for persistence of the Wassermann reaction in spite of treatment. The relative isolation of spirochætal foci from the blood stream in aortitis and neuro-syphilis is already established, and may reasonably be regarded as one cause for persistence of the Wassermann reaction. It may prove to be the sole cause, but at present it would be wrong to be dogmatic.

Colonel Burke has raised the question of spirochætal immunity to anti-syphilitic remedies. It is an interesting and legitimate question, but, as yet, is at an entirely theoretical level, for there is no evidence to justify the acceptance of such a view.

Late syphilitic affections usually do not run a steadily progressive course, as judged either clinically or serologically ; and there is a well-recognised small group of tabetics in which the patients become worse in spite of negative Wassermann reactions in both blood and cerebro-spinal fluid. In such cases the spirochætal foci may possibly be completely shut off from the blood stream. At the same time, a possible, although again theoretical, explanation may be failure of the individual to react against the infection.

Pyro-therapy, an example of empiricism founded on good clinical observation, has proved to be successful in a proportion of cases of Wassermann-fast syphilis. The best results from its use have, of course, been in the treatment of G.P.I., for which it was first employed. In the speaker's experience, it had been less valuable in cases of tabes resistant to ordinary methods of treatment, but he felt that as yet it had not been given a sufficiently long trial. For syphilitic optic atrophy it might also be tried, for, as is well known, vision as a rule cannot be preserved by the more orthodox methods of treatment. He had apparent success in one progressive case in which the Wassermann reaction in blood and cerebro-spinal fluid was negative.

Mr. F. FOWLER WARD felt grateful to Colonel Burke for having brought forward for discussion a subject which was the bugbear of syphilitic practice, the Wassermann-fast case. Looking at the standard course of treatment, it seemed to the speaker that the people who had a persisting positive were liable to everlasting injections of some sort. But patients would not tolerate that. His

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own experience had taught him that one could give too much arsenobenzene. He used N.A.B. and bismuth. A patient was brought to a certain stage, his health was good, therefore why make him worse, as one might, by giving him more arsenical injections? The serological reaction was only one evidence in a chain of symptoms, and it did not seem reasonable to go on over-treating a patient because of one serological reaction, especially as the general health suffered in the process. For some time he used stabilarsan, but he found that patients got symptoms after it, such as malaise, and that discouraged them from coming up for treatment. He did not regard a Wassermann-fast condition as something which one must always be interfering with. If such a patient had been otherwise well for ten years, the speaker did not believe in always worrying him in efforts to get the Wassermann negative.

Dr. B. B. SHARP said he agreed with Colonel Harrison's remark that the most inveterate cases of Wassermann-fastness were those who had had no treatment at all. As a working hypothesis he had felt that when a patient presented himself for the first time for treatment who had had (probably) syphilis ten years ago or more, and had had a positive Wassermann for that period, it was improbable that, whatever was done for him, one would permanently secure a negative Wassermann in him. And he did not think one should frighten such a patient too much about his Wassermann. It was necessary to hold the balance between the patient and the disease, otherwise there was a danger of giving a man a phobia about his disease, especially as, without prolonged treatment, he might live long and feel well. A man should be treated at first energetically, and if that did not produce the desired effect he should have a short course of treatment once a year and be given a chance of living his normal life. Otherwise he would be anxious and miserable to the end of his days.

He agreed as to the rarity of jaundice and nephritis after giving these drugs; the cases of jaundice he had had in the last few years could be counted on the fingers of one hand. The jaundice in those cases was not due to the arsenic itself, but to the benzene radical. That being so, it would be a surprise to find it resulting from the administration of bismuth drugs, which did not contain it.

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As to graduated or quantitative Wassermann estimations during treatment, he thought the most exact available at present was the Verne's test, as it gave the greatest possible number of graduations, and was the most accurately controlled of the precipitation tests, ranging as it did from 0 to 200 units, anything over 4 being regarded as positive. And in regard to precipitation tests, such as Kahn's, the Wassermann usually became negative during treatment before the precipitation test became negative.

It had struck him that perhaps too much stress was laid on these graduated Wassermann reactions during treatment.

The strength of the reaction was not entirely due to the number of spirochætes being destroyed. It could be presumed that the strength of the Wassermann reaction depended on the strength of the patient's ability to react. But his tissues were being bombarded with other things, which might exhaust their capacity to produce an antibody, and might reduce the capacity to produce a syphilis antibody. If therefore the patient were given a rest, the Wassermann might become positive once more.

Dr. H. M. HANSHELL congratulated Colonel Burke on his paper, and expressed his high appreciation of it. He noted that Colonel Burke had watched a large number of cases of primary and secondary syphilis for a period of years after completion of treatment by his alternate method. They had remained blood-Wassermann negative and clinically free of signs of syphilis. On the other hand, Colonel Harrison reported identically happy results in a large number of his own cases, after treatment by the concurrent method. He (Dr. Hanshell) had always given the concurrent treatment. But he now concluded that it did not matter which method was adopted, so long as enough was given; certainly the concurrent method saved time. His own clinical experience was strongly against the hypothesis that continuous "concurrent treatment produced drug-fast spirochaemes as evidenced by Wassermann positive inveteracy." In fact, the persistent Wassermann cases had given a history of no treatment in the primary or secondary stages, or of only trivial treatment: and his success in making these cases Wassermann negative had been only in those few who had received continuous concurrent treatment,

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without break, even though this had meant forty or fifty consecutive weeks of injections with unchanged drugs. Slow or bad eliminators were, happily, rare ; if poisoned they, of course, needed rest from the poison. But once their tolerable dose had been ascertained no rest need be given. But many patients needed continuous adjuvant treatment, *e.g.*, with cod-liver oil.

Dr. H. C. G. SEMON congratulated Colonel Burke on a most able paper, in which he satisfied most of his hearers that he had a remedy for every stage of the disease, even for congenital syphilis.

He had a shot to add to Colonel Harrison's locker as to concurrent and alternating treatment. If, as was known, arsenobenzene was excreted within two days of its infection, there must be four days in the early stages in which nothing was happening. And that was a very important period, for during it the spirochæte was more or less unmolested and could get into the central nervous system. That favoured the giving concurrently of a substance with the arsenobenzol which was not so quickly excreted, such as bismuth.

As to the incidence of jaundice being more frequent in cases in which concurrent treatment had been given ; according to Colonel Burke that might be so, but personally he had never seen a case of jaundice during a bismuth course alone. And it would be against the view that a benzene radical was responsible for the damage to the liver. Bismuth was more liable to act on the kidneys. If jaundice did ensue in those cases, it was generally slight in degree, and might be promptly cleared up by arsenic treatment. It was, therefore, a true syphilitic jaundice, and not due to drug administration.

Dr. MARGARET RORKE said that she was concerned with one particular type of case, in women only ; she did not see the variety which were met with in mixed clinics. She had found Colonel Burke's paper very helpful, and the whole question was, to her, of great personal interest. Women did not seek treatment for their syphilis so early as did men, two causes of this being, she thought, ignorance and shame on the women's part. When hearing of Colonel Burke's early cases, therefore, she thought of the few cases she saw of his categories 1 and 2. It was considered, in her clinic, to be an early case if it had a florid secondary rash. A great number of the cases at her

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clinic were instances of well-established secondary syphilis or syphilis associated with pregnancy and a history of still-birth. The old gummatous cases were dumped on the department in a marvellous way. Therefore, there were many Wassermann-fast cases to be found in a women's V.D. clinic.

Colonel Burke had remarked that he did not expect every one to agree with him, but she agreed with him on many points. One was that to exhibit different preparations of the drugs used for syphilis was a very useful thing. To put into the patient the same drugs time after time was unimaginative, for it was obvious that after a time the tissues would fail to react to them properly, and in later stages a Wassermann-fast condition was sure to be reached. She would like to see the correct therapeutic doses worked out in respect of most of the metals, such as barium, etc. In these cases she had been glad to use silver salvarsan and parallel substances, as well as iodides.

She was particularly interested in some of the later stages, such as 5 and 6. The reader had stressed the importance of imposing a rest period in administering iodide of potassium. She had seen patients who had come as later cases, who had had considerable treatment, though nothing like the real treatment, whose symptoms were relieved, but who, from a variety of causes, lapsed treatment. The Wassermann was persistently positive, and the patient returned nine or eighteen months later because she had presented herself in another department of the hospital and was sent on to the clinic again. After that rest period one frequently saw that the Wassermann was negative. She wondered whether that was because, in the interval without treatment, the patient's resistance has been raised.

She would like to know whether Colonel Burke succeeded in getting the people in classes 5 and 6 to attend regularly for fifty-four or fifty-six weeks. Her experience was that some of these patients stood a certain amount of treatment very well, but that after a certain point they developed minor disabilities, *i.e.*, gastro-intestinal or mouth trouble, or a mild albuminuria. Some went downhill and became thin and anæmic. By the time one saw some of these tertiary cases in women they were far from fit; they had become jaded by frequent child-bearing, and some had habitually taken too little food.

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She agreed that the early cases should be saturated with treatment, *i.e.*, to the limit of their power of absorption. The lesser case one could deal with more gently, otherwise there would be a tendency to precipitate illness.

She desired to see the Wassermann become negative in all cases, but she had her doubts whether some of the old-standing cases would ever be made persistently negative. She was accustomed to tell her students that a negative Wassermann was very good, but that it was better to have a case with a positive Wassermann than one which in the process of becoming negative killed the patient.

The PRESIDENT considered that the discussion had been a very interesting one, and that the various differences of opinion expressed rather emphasised the warning that one must not be too dogmatic on any aspect of the treatment of syphilis at the present time. There had been revealed, too, considerable difference of opinion as to what did cure syphilis, whether it was the drug, or the response of the tissues to the stimulus which the drug gave them. He agreed with Colonel Burke when he said it was not the drug which had a spirochæticidal effect, but that a substance was produced by the reaction of the tissues which stopped the evil effects of the spirochæte's activity. There seemed to have been much in what was put forward which tended to confirm that idea. If that was so, it seemed sound to suggest that ringing the changes on drugs might be useful. For after a time a particular drug might fail to have the same effect as at first. That was why the pyrogenic action might be useful as a stimulus to tissue metabolism, enabling the tissues to produce a body which had an effect on the spirochæte.

The other matter concerned the nourishment of the patient, a point which was touched on by Dr. Margaret Rorke. He was aware that some who were treating syphilis recognised the importance of keeping up the patient's nourishment, but some did not pay as much attention to that as they well might. If a patient was not nourished enough, it was possible that the tissues would fail to respond to the drugs which were being given. It might be held that analogy from other diseases was a mistake, but was one on sound lines in feeling that the end of all anti-syphilitic treatment was to produce a negative Wassermann reaction? In the case of tubercu-

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losis, which had some similarities to syphilis, one did not expect, by any treatment, to get rid of the positive tuberculin reaction, and while that reaction remained positive the general condition of the patient might be such as to warrant the idea that he was cured. Germs of syphilis might remain in the tissues without necessarily causing evil effects. He felt some sympathy with Dr. Sharp and Mr. Fowler Ward that it was carrying the matter too far if treatment was so severe that it resulted in the patient becoming ill, or if he were thereby rendered miserable, and possibly became a syphiliphobiatic.

The discussion would have served a useful purpose if it led to this subject being viewed on broad and general lines, in the hope that at a future date a conclusion would be arrived at which was both sound and wise.

Colonel BURKE in his reply wished to thank the members for the courteous manner in which his somewhat controversial paper had been received. The discussion had been both interesting and stimulating. Many different opinions had been expressed ; and it was only by the thorough airing of such differences that progress was made and stagnation avoided.

In his reply to Colonel Harrison he had to state that in his records of cases treated by the alternating method, there were, from 1920 to 1927, seventy-one patients who completed the course according to schedule ; and from 1928 to 1930 there were sixty-five. That made a total of 136 ; and among these there had been no instance of clinical or serological relapse. In Colonel Harrison's recent valuable report, published under the auspices of the Medical Research Council, there were recorded 145 cases who had completed the course laid down in Treatment Groups IV. and V., according to the concurrent principle ; and among these there were eight relapses.

He agreed that treatment with one agent alone—be it arsenobenzene, bismuth or mercury—was essentially bad practice. He, personally, was not convinced that anything had yet been produced to show that arsenobenzene specially conduced to early involvement of the central nervous system. The true position seemed to him to be that the chief causal factor in the production of neurosyphilis and visceral syphilis was not so much the agent used, but the inadequate amount of it that it was possible to administer within a certain time-limit. Colonel

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Harrison had referred to the cases analysed. Out of the 280 cases investigated who were suffering from some form of neuro-syphilis, less than 20 per cent. had received any treatment during the primary and secondary stages. About 80 per cent. of these neuro-syphilitics had therefore received no treatment whatever. The incidence of neuro-syphilis was thus very much higher among untreated individuals. The main feature of the treated cases was the utter inadequacy of the treatment given, both in respect of amount and duration. It appeared to him, then, that the causes of neuro-syphilis were, in order of frequency : (1) no treatment ; and (2) inadequate treatment by any remedial agent, especially if one only were used. It would be found that the effect of treatment by either bismuth or mercury alone would, so far as the central nervous and visceral systems are concerned, be exactly the same as for arsenobenzene alone. It seemed to be an impossibility to give adequate treatment by means of only one remedial agent. Prolonged use exhausted the reactive power of the tissues, and intervals of rest had to be instituted to avoid poisoning the patient. The end result was that the parasite sought refuge in inaccessible sites, and was given time to entrench itself therein. He thought that perhaps too much stress had been laid upon neuro-recurrences, and not enough on cardiovascular and other visceral involvement, although these might be longer in appearing above the clinical horizon.

Colonel Harrison and he had been at loggerheads for a long time over the matter of concurrent *versus* alternating treatment. Colonel Burke could not agree that by starting treatment with arsenobenzene alone one gave the parasite several days' start in the central nervous system, because there was no evidence that by combining arsenobenzene with, say, mercury, a barrier was set up between that system and the parasite. Neuro-syphilis was by no means unknown in the pre-salvarsan era. The argument advanced by Colonel Harrison, if carried right to its logical conclusion, implied that one should give not only arsenobenzene and bismuth simultaneously, but also use mercury at the same time ; and, if a hundred more remedial agents were available, they should all be exhibited together. With reference to the Moore and Kemp analysis, the main feature present in their cases of

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neuro-recurrence was the inadequacy of treatment. Where the treatment was inadequate—in accordance with their Treatment Group No. IV.—of the seventy-one patients in this group, none developed a neuro-recurrence.

Colonel Burke's method was similar to that of Moore and Kemp ; but while they found among their defaulters fifty-nine neuro-recurrences, he had found none in his own series. One reason might be that his clinical acumen and that of his staff was not so high as that at the Johns Hopkins Hospital ; but it was more likely that the result was due to the fact that, while Moore and Kemp had used mercury, he had used the more potent bismuth.

The patients seemed to default earlier in the Moore and Kemp series than in his own. It was exceedingly rare for him to have a defaulter in the first eight weeks, *i.e.*, after having received arsenobenzene only. It seemed possible that a reason for their early defaulting was the use of "606," and not "914." American seamen attending Colonel Burke's clinic frequently stated that they had been very ill after their "shot of 606" in U.S.A. Again, it may be that "606" has a greater tendency to cause, for example, cranial nerve palsy than has "914."

Taking the Moore and Kemp series, the position appeared to be that, under the alternating principle, the patient who defaults before the second drug has been given is more likely to develop a neuro-recurrence than is one who defaults at a later stage. It is important to note, however, in connection with the American cases, that 97 per cent. of the neuro-recurrences occurred within six months of defaulting—that the neuro-recurrence brought them back early. He suggested that under the concurrent method a person who defaults in the same time—after, say, eight injections of arsenobenzene and eight of bismuth—is, although he may have no neuro-recurrence, most certainly not cured of his syphilis. The chances are that he is still infectious, that he will suffer a Wassermann-relapse, may be Wassermann-fast, and years after may show clinical signs of visceral or central nervous system damage. Treatment would appear to consist of making a choice between two evils—the concurrent evil and the alternating evil. Default under either results in failure to cure. Is it more disastrous under the one that the uncuredness may manifest itself early as a neuro-recurrence?

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rence which will drive the patient to resume treatment, or that under the concurrent method the uncuredness should remain hidden for perhaps many years? It should be borne in mind that it is not reasonable either to bless or damn a particular method by the results occurring to patients who do not carry out the method properly.

With respect to Colonel Harrison's remarks about the giving of silver-salvarsan being a double bombardment, he did not agree. The combination of silver with arsenobenzene is an attempt to combine the specific effect of the arseno compound with the general antiseptic action of the silver ion.

The arseno group exerts its antisyphilitic effect by virtue of the reaction of the patient's tissues. The silver, on the other hand, acts directly as an antiseptic. The two in combination do not therefore entail a double bombardment of the tissues with the consequent risk of their exhaustion. Lenhoff-Wyld held that the combination of sulfarsenol with another metal resulted in an increased therapeutic value. He found that the most suitable metal was zinc. But zinc has no specific effect upon the *Treponema pallidum*. Bismuth has. There is no objection to the use of another metal, provided it has no similar tissue reaction to that of arsenobenzene or bismuth, and causes no extra load to be thrown on organs such as the liver and kidneys. The danger of tipping your arrows with two or more poisons is that they may actually counteract one another, especially since these poisons do not act directly upon the parasite. By tipping your arrows with two or more poisons you may be very successful in destroying your patient, or causing him grave damage.

Colonel Burke would direct Colonel Harrison's attention to the experiments of Akatsu and Noguchi, which demonstrated that the parasite could become drug resistant.

He personally was of the opinion that the most inveterate cases of Wassermann-fastness were those who had been inadequately treated. A patient who has not had his syphilis treated at all was, he agreed, difficult to cure, and for the reason adduced by Colonel Harrison—the inaccessibility of the parasite. Such cases, however, could not be called Wassermann-fast until such time as they had received, in his opinion, two years of treatment in accordance with the scheme laid down in his Course V.

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These patients did not, he thought, come within the definition he had made in his paper.

Colonel Burke thought that a quantitative serological test was of great value. His experience was that an alteration of strength of reaction of a patient's serum in the absence of treatment was uncommon enough to make a graduated test extremely useful.

When he began to see cases of neuro-syphilis occurring more frequently under his method than under Colonel Harrison's, then he would willingly strike his flag, but in the meantime, since he had had an equal freedom from neuro-recurrence and a greater freedom from other relapses than had the advocates of concurrency, he must still keep it flying.

In reply to Dr. Anwyl Davies, he had to state that he had no experience of the value of sodium theosulphate in changing a positive Wassermann into a negative. He rated protein-shock therapy, however, very highly in this respect, although he had found that one preliminary effect of it might be provocative or to convert a + reaction into a +— one. Anti-specific treatment thereafter was extraordinarily successful.

He was extremely interested in Dr. Riddock's remarks. He had already referred to the experimental work of Akatsu and Noguchi, and of Klauder with respect to the parasite developing drug-resistance. He would point out that every clinical case, carefully studied and controlled, was an experiment; and the evidence it provided and the deductions made from it were just as valid as the research conducted in a test-tube or upon the experimental animal.

Colonel Burke agreed with Mr. Fowler Ward that a case of Wassermann-fastness could be overtreated. There was no use burning down Moscow in order to get rid of an invader who was not doing much damage. It was for this reason that he had tried to emphasise the necessity for a very thorough clinical examination of a patient who was Wassermann-fast. The result of such an examination might be absolutely to contra-indicate anti-syphilitic treatment.

Dr. Sharp assumed that jaundice occurring during treatment was only due to the benzene radicle in the arsenobenzol. For himself he was convinced of the occurrence of bismuth jaundice. Hudelo and Rabut

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called attention to it in 1924. More recently, Lafourcade, Fouquet and Nativelle (*Bull. Soc. Franc. de Derm. et de Syph.*, November, 1929) showed that jaundice does occur in patients who have never had arsenobenzol, and in their experience it is not more frequent after arsenical treatment than after the administration of bismuth or mercury. He had to differ from Dr. Sharp as to the cause of jaundice after arsenobenzol. This was surely due to the arsenic, and not to the benzene group. The liver is well known to be a great store-house for arsenic, and there has been a good deal of work done to show that the hepatic damage is wrought by the elemental arsenic. Colonel Burke thought that we must accept the degree of complement fixation as a good practical index of the amount of treponemal activity, and it was on that account that he thought there was a distinct advantage in measuring the strength of the reaction.

Dr. Hanschell and he were in agreement in this at least, that they both realised that whatever method of treatment was adopted, enough of it had to be given. His own view was that by the concurrent method you could not give enough without at the same time damaging the patient. Dr. Hanschell's series of seventy-three primary cases was interesting, because all had received concurrent treatment with eight injections of arsenobenzol and eight of bismuth. Yet none of these had suffered any relapse clinically or serologically. Personally he could not feel satisfied that these patients were cured, and he felt that this was exactly the type of case which showed the lesions of visceral syphilis described by Warthin. He was glad to find that Dr. Hanschell had had such good results with protein-shock therapy in Wassermann-fast cases.

He did not quite see the point that Dr. Semon was making by his reference to arsenobenzol being excreted in two days. Surely that was not the case. At least 50 per cent. of the dose was stored in the body for a period of weeks. The actual arsenobenzol excreted was probably that part of the dose which the tissues had not used therapeutically. Again, Dr. Semon mentioned the benzene radical as being the cause of jaundice. With that he did not agree. Certainly he had seen recently many cases of jaundice which could not be attributed to syphilis, catarrh, or arsenobenzol, but which were apparently true cases of bismuth jaundice.

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He agreed with Dr. Rorke that syphilis in women presented many more difficult problems than in men. He thought it would be extremely useful if other heavy metals were investigated with regard to treatment of syphilis, and especially those elements in Group V. of the periodic table. His patients on Courses V. and VI. attended very well indeed. It was carefully explained to them on their first visit how long treatment would last.

His own practice was, in all cases, but especially in the later stages of the disease, to combine anti-syphilitic treatment with the exhibition of tonics. Vitamins, light-therapy, Easton's syrup, cod liver oil, and so on, were all most valuable; the patient had to be treated as well as his or her disease.

In conclusion, Colonel Burke wished again to express to the President and those who had taken part in the discussion his sincere thanks.